THE MERCK INDEX

AN ENCYCLOPEDIA OF CHEMICALS AND DRUGS

NINTH EDITION

Martha Windholz, Editor
Susan Budavari, Associate Editor
Lorraine Y. Stroumtsos, Assistant Editor
Margaret Noether Fertig, Assistant Editor

Published by

MERCK & CO., INC.

RAHWAY, N.J., U.S.A.

1976

EXHIBIT A

ration of isomers: Bedford, Richardson, Nature 212, 733 (1966); Harper et al. Brit. pat. 1,064,629; Fr. Addn. pat. 90,418 (both 1967 to I.C.I.). Comparative activity of isomers: Harper, Walpole, Nature 212, 87 (1966). Pharmacology: eidem, J. Endocrinol. 37, 83 (1967); J. Reprod. Fert. 13, ogy: eidem, J. Endocrinol. 37, 83 (1967); J. Reprod. Fert. 13, 101 (1967); Terenius, Acta Endocrinol. (Copenhagen) 64, 47 (1970).

Crystals from petr ether, mp 96-98°. Citrate, C₃₃H₃₇NO₁₀ ICI-46474, Nolvadex. mp 140-142°. cis-Form base, mp 72-74° from methanol. cis-Form citrate, C₃₃H₃₇NO₁₀ ICI-47699. mp 126-128°. THERAP CAT: Anti-estrogen.

8824. Tanacetin. Decahydro-6β, 9aα-dihydroxy-5aβ-methyl-3, 9-bis(methylene)naphtho[1, 2-b]furan-2(3H)-one; 1β, 5α-dihydroxy-6β, 7αH-selina-4(15), 11(13)-dien-6, 12-olide. C₁₃H₂₀O; mol wt 264.31. C 68.16%, H 7.63%, O 24.21%. Isoln from seed, herb, and flowers of Tanacetum vulgare L., Compositae: Homolle, J. Pharm. Chim. 7, 57 (1845); Jaretzky, Kühne, Arch. Pharm. 271, 353 (1933); Suchy, Coll. Czech. Chem. Commun. 27, 1058 (1962). Structure and absolute config: Samek et al., ibid. 38, 1971 (1973).

Crystals, mp 205°. $[\alpha]_D^{22} + 179.5$ ° (c = 2.3 in ethanol).

8825. Tanganil. N-Acetylleucine compound with 2-ami-noethanol; monoethanolamine DL-acetylleucinate; DL-acetylnoethanol; monoethanolamine bl-acetyleucine monoethanolamine salt of α -acetamidoisocaproic acid; RP 7452. $C_{10}H_{22}N_{1}O_{4}$; mol wt 234.29. C 51.26%, H 9.46%, N 11.96%, O 27.32%. Prepn: Gailliot et al., U.S. pat. 2,941,924 (1960 to Rhône-Poulenc).

$(c\mathbf{H}_3)_2$ сиси $_2$ сисоон. \mathbf{H}_2 иси $_2$ си инсоси3

Crystals, mp about 150°. Soly in water: >20%; soly in alcohol: ~1%. pH of 10% aq soln: about 6. > 20%; slight THERAP CAT: Antivertigo agent.

8826. Tanghinigenin. 7β,8-Epoxy-3β,14-dihydroxy-5β-card-20(22)-enolide. C₂₃H₃₂O₅; mol wt 388.49. C 71.10%, H 8.30%, O 20.59%. Isoln from glucosides: Sigg et al., Helv. Chim. Acta 38, 166 (1955). Structure: Flury, Reichstein, Ann. Chim. (Rome) 53, 23 (1963); Flury et al., Helv. Chim. Acta 48, 1113 (1965).

Prisms from acetone + petr ether, mp 187-188°. +14.1° (c = 1.138 in chloroform). uv max: 217 nm (log e 4.22). LD₅₀ in cats: 1 mg/kg i.v., Chen, Henderson, J. Pharmacol. Exp. Ther. 111, 365 (1954).

Acetate, C₁₃H₃₄O₆ acetyltanghinigenin. Prisms from acetone + petr ether, mp 241-243°. [a]₂₅²⁵ +14.9° (c = 1.075 in chloroform)

chloroform).

8827. Tanghinin. 3\(\beta\)-[(2-O-Acetyl-6-deoxy-3-O-methyl-a-L-glucopyranosyl)oxy]-7\(\beta\),8-epoxy-14-hydroxy-5\(\beta\)-eard-20(22)-enolide. C₃₁H₄₆O₁₀; mol wt 590.69. C 65.06%, H 7.85%, O 27.09%. From the seed of Tanghinia madagascariensis Pet., Apocynaceae and Tanghinia venenifera Poir. Apocynaceae. Isoln: Arnaud, Compt. Rend. 108, 1255 (1889); Frèrejacque et al., ibid. 226, 268 (1948). Tentative structure: Sigg et al., Helv. Chim. Acta 38, 166 (1955). Revised structure: Flury, Reichstein, Ann. Chim. (Rome) 53, 23 (1963). ture: Flury, Reichstein, Ann. Chim. (Rome) 53, 23 (1963).

Leaflets from methanol + ether, mp 128-131°. Leaises from methanol + ether, mp 128-131. [α] $_D^{\rm in}$ - 81.5° (c = 1.092 in methanol). uv spectra: Frèrejacque et al., Helv. Chim. Acta 39, 1900 (1956). LD₅₀ in cats: 0.4 mg/kg i.v., Chen, Henderson, J. Pharmacol. Exp. Ther. 111, 365 (1954).

8828. Tannic Acid. Tannin; gallotannin; gallotannic acid. Incorrectly "digallic acid". Tannic acid of commerce usually contains about 10% H₂O. Occurs in the bark and usually contains about 10% H₂O. Occurs in the bark and fruit of many plants, notably in the bark of the oak species, in sumac and myrobalan. It is produced from Turkish or Chinese nutgall, the former contg 50-60%, the latter about 70%. The chemistry of the tannins is most complex and non-uniform. Tannins may be divided into 2 groups: (a) derivatives of flavanols, so-called condensed tannins and (b) hydrolyzable tannins (the more important group) which are esters of a sugar, usually glucose, with one or more trihydroxybenzenecarboxylic acids. The structure given here is that oxyoenzenecarooxylic acids. The structure given here is that of a tannin named corilagin: Schmidt et al., Ann. 587, 67 (1954). The empirical formula of corilagin is $C_{77}H_{14}O_{15}$. For the commercial tannic acid, whose specifications follow, the empirical formula is usually given as $C_{76}H_{57}O_{46}$. Comprehensive reviews: M. Nierenstein, The Natural Organic Tan-

nins (London, 1934); O. Th. Schmidt, "Gallotannine" in Fortschr. Chem. Org. Naturst. 13, 70-136 (1956); Symposium on the Chemistry of Vegetable Tannins (Soc. Leather Trades Chemists, Croydon 1956).

Yellowish-white to light brown, amorphous, bulky pow Yellowish-white to light brown, amorphous, bulky powder or flakes, or spongy masses; faint characteristic odor; astringent taste. Gradually darkens on exposure to air and light; at 210-215' dec mostly into pyrogallol and CO. Gives insol ppts with albumin, starch, gelatin, most alkaloidal and metallic salts; produces a bluish-black color or precip with ferric salts. One gram dissolves in 0.35 ml water, 1 ml warm glycerol; very sol in alle acceptant processing. precip with terrie sairs. One grain dissolves in 0.35 ml warter, 1 ml warm glycerol; very sol in alc, acetone; practically insol in benzene, chloroform, ether, petr ether, carbon disulfide, carbon tetrachloride. Keep well closed and protected from light. LD₁₀₀ orally in mice: 6.0 g/kg, Robinson, Graessle, J. Pharmacol Exp. Ther. 77, 63 (1943).

Incompat: Salts of heavy metals, alkaloids, gelatin, albuniated by the carbon statement of the compact of the compact of the carbon statement of the carbon state

min, starch, oxidizing substances-e.g., permanganates,

chlorates; spirit nitrous ether, lime water.

USE: Mordant in dyeing; manuf ink; sizing paper and silk; printing fabrics; with gelatin and albumin for manuf of imitation horn and tortoise shell; tanning; clarifying beer or wine; in photography; as coagulant in rubber manuf; manuf gallic acid and pyrogallol; as reagent in analytical chemistry. THERAP CAT: Astringent.

THERAP CAT (VET): Astringent, hemostatic, in solutions for burns. Has been used internally as an astringent and as a heavy metal antidote.

8829. Tannoform. Methyleneditannin; tannin-formaldehyde; Helgotan. Prepd by condensing one mole formaldehyde with two moles tannin: Chemnitius, Pharm. Zentralh. 68, 273 (1927); Schwyzer, Pharm. Ztg. 74, 1334 (1929).

Reddish, odorless, tasteless, bulky powder, mp about 2300 Practically insol in water; sol in alcohol. with decompn.

THERAP CAT: Astringent.

THERAF CAT (VET): Externally as astringent, antiseptic (skin lesions and otorrhea). Has been used internally for diarrhea.

8830. Tanphetamin. d-Amphetamine tannate; Synatan A 17.5 mg dose is equivalent to 4.98 mg of d-amphetamine base. Prepd by the reaction of d-amphetamine (free base) with tannic acid in isopropanol: Cavallito, U.S. pat. 2,950,-309 (1960 to Irwin, Neisler and Co.).

Caution: Excessive use may lead to tolerance and physical dependence

THERAP CAT: Adrenergic.

8831. Tantalum. Ta; at. wt 180.9479; at. no. 73; valence 5, also 4, 3, 2. Two naturally occurring isotopes: 181 (99.9877%); 180 (0.0123%; $T_{\rm v} > 10^{12}$ years); artificial radioactive isotopes: 172-179; 182-186. Occurs almost invariactive isotopes: 172-179; 182-186. Occurs almost invariably with niobium; less abundant than niobium. Found in the minerals columbite (q.v.), tantalite [(Fe,Mn)(Ta,Nb)₂O₆] and microlite [(Na,Ca)₂Ta₂O₆(O,OH,F)]. Discovered by Ekeberg in 1802; first obtained pure by Bolton: Z. Elektrochem. 11, 45 (1905). Prepn: Schoeller, Powell, J. Chem. Soc. 119, 1927 (1921). Reviews of tantalum and its compounds: G. L. Miller, Tantalum and Niobium (Academic Press, New York, 1959) 767 pp; Brown, "The Chemistry of Niobium and Tantalum" in Comprehensive Inorganic Chemistry vol. 3, J. C. Bailar. Jr. et al. Eds. (Pergamon Press, Oxford, 1973) J. C. Bailar, Jr. et al., Eds. (Pergamon Press, Oxford, 1973)

pp 553-622.
Gray, very hard, malleable, ductile metal; can readily be drawn in fine wires. drawn in fine wires. mp 2996°. bp 5429°. d 16.69. Spec heat (0°): 0.036 cal/g/°C. Electrical resistivity (18°): 12.4 sohm-cm. Insol in water. Very resistant to chemical attack; not attacked by acids other than hydrofluoric; not attacked by aq alkalies; slowly attacked by fused alkalies. Reacts with fluorine, chlorine, and oxygen only on heating. At high temps absorbs several hundred times its volume of hydro-

gen; combines with nitrogen, with carbon.
USE: In pen points; analytical weights; apparatus and instruments for chemical, surgical, and dental use instead of platinum, in tantalum capacitors (a type of electrolytic con-denser, trademarked "Tantalytic").

THERAP CAT: Surgical aid.

8832. Tantalum Pentachloride. Cl_5Ta ; mol wt 358.24. $Cl_49.50\%$, $Ta_50.50\%$. $TaCl_5$. Prepn: Rolsten, J. Am.

Chem. Soc. 80, 2952 (1958). Review of tantalum halides: Fairbrother in Halogen Chemistry vol. 3, V. Gutmann, Ed. (Academic Press, New York, 1967) pp 123-178.

White or light yellow, cryst powder; monoclinic; dec in moist air. d 3.68; mp 216.5-220°. Begins to volatilize at 144°, bp 239.3°. Dec by water; sol in abs alcohol. LD₅₀ orally in rats: 1.9 g/kg.

8833. Tantalum Pentafluoride. F₅Ta; mol wt 275.95, F 34.43%, Ta 65.57%. TaF₅. Prepd from tantalum pentachloride by the halide exchange method according to the equaride by the halide exchange method according to the equation TaCl₅ +5HF \rightarrow TaF₅. +5HCl: Ruff, Zedner, Ber. 42, 492 (1909); Ruff, Schiller, Z. Anorg. Allgem. Chem. 72, 329 (1911); Kwasnik in Handbook of Preparative Inorganic Chemistry vol. 1, G. Brauer, Ed. (Academic Press, New York, 2nd ed. 1963) pp 255-256. Prepn from the elements: Pairbrother, Frith, J. Chem. Soc. 1951, 3051. Review of transition metal pentafluorides: Peacock, Advan. Fluoride Chem. 7, 113-145 (1973).

Deliquescent, strongly refractive prisms. 429 A 74. mp.

Deliquescent, strongly refractive prisms. d²⁰ 4.74. mp 96.8°. Also reported as 95.1°: Fairbrother, Frith, *loc. cit.* bp 229.5°. Sol in water and ether with formation of oxyfluoro complexes. Also sol in coned nitric acid, more sol in fuming nitric acid. Sparingly sol in hot carbon disulfide and hot carbon tetrachloride. Etches glass slowly.

USE: Friedel-Crafts catalyst.

8834. Tantalum Pentoxide. Tantalic acid anhydride. O₅Ta₂, mol wt 441.90. O 18.10%, Ta 81.89%. Ta₂O₅. White, microcryst, infusible powder. Insol in water, alcohol, mineral acids; sol in HF; dec by fusing with KHSO₄ or KOH, forming potassium tantalate with the latter. LD₅₀ orally in rats: > 8.0 g/kg.

8835. Tar Acids. Tar acids are the phenols obtained from coal tar distillates or synthesized from coal tar hydrocar-bons. Examples: Phenol, cresol, cresylic acid, xylenol.

8836. Taraxacum. Dandelion; lion's tooth. Dried rhizome and roots of Taraxacum palustre (Lyons) Lam. & DC. (T. officinale Weber, Leontodon taraxacum L.), Compositae. Habit. Europe; naturalized in North America. Constit. Taraxerol, choline, levulin, inulin, pectin.

8837. Taraxasterol. 18a.19a-Urs-20(30)-en-38-ol: ta-8837. Taraxasterol. 18α, 19α-Urs-20(30)-en-3β-ol; taraxast-20(30)-en-3β-ol; anthesterin; α-lactucerol; taraxasterin. C₃₀H₅₀O; mol wt 426.70. C 84.44%, H 11.81%, O 3.75%. A monohydroxy triterpene. Isoln from Taraxacum officinale, Wiggers, Compositae: Power, Browning, J. Chem. Soc. 101, 2411 (1912). Structure and configuration: Ames et al., ibid. 1954, 1905. Identity with anthesterin: Power, Browning ibid. 105, 1829 (1914); with α-lactucerol: Zellner, Monatsh. 47, 681 (1926).

Needles from alcohol, mp 221-222°. $[\alpha]_D$ +96.3° (CHCl₃). Very sol in alcohol, ether, petr ether; slightly sol in chloroform, benzene, carbon disulfide, acetone. Acetate, $C_{32}H_{32}O_2$, lactucerin, lactucon. Hexagonal plates. mp 251-252° (from ethyl acetate + alcohol). $[\alpha]_D$ + 100.5°.

8838. Taraxein. A protein complex isolated from the blood serum of schizophrenics by chromatography on diethblood serum of schizophrenics by chromatography on diethylaminoethyl cellulose. The taraxein fraction precedes the ceruloplasmin fraction. Contains copper bound to protein. Method of isolation: Heath et al., Am. J. Psychiat. 114, 14 (1957); (Lippincott's) Medical Science 6, 401 (1959). Processing and identification: Heath et al., Proc. 3rd World Congr. Psychiat., Montreal. 1961 1, 619 (1962). Studies of